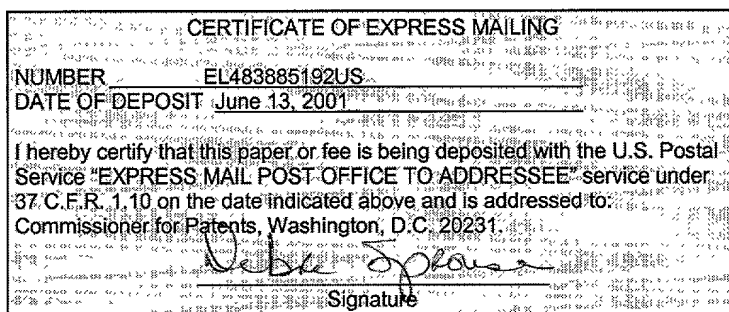


IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: §
Burgess et al. § Group Art Unit: Not assigned
Serial No.: Not assigned § Examiner: Not assigned
Filed: June 13, 2001 § Atty Docket: 017575.0661
For: METHODS OF LABELLING § Client Docket: TAMUS1277
BIOMOLECULES WITH §
FLUORESCENT DYES §

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231



Sir:

Please amend this application as follows:

IN THE SPECIFICATION:

Please replace the title with the following title:

--METHODS OF LABELLING BIOMOLECULES WITH FLUORESCENT DYES--.

Please amend the Specification by deleting the paragraph identified below and replacing it with the following paragraph. Pursuant to 37 C.F.R. 1.121(b), attached at the end of this document are marked up versions of the replacement paragraphs showing the amendments.

Please delete the paragraph at page 1, lines 8 - 11, and replace it with the following paragraph:

--This application is a divisional application of co-pending U.S. Patent Application Serial No. 09/430,718 filed on December 14, 1999, which claims the benefit of United States

Provisional Patent Application entitled "Through Bond Energy Transfer in Fluorescent Dyes for Labelling Biological Molecules," Serial No. 60/112,711 filed December 18, 1998.--

IN THE CLAIMS:

Please cancel claims 1-12 without prejudice.

Please add the following new claims:

- 13. A method of preparing a fluorescent dye useful to attach to a biomolecule, the method comprising:
- providing a UV absorbing chromophore;
 - providing a fluorescent emitter; and
 - linking the chromophore and emitter to prepare the fluorescent dye; wherein:
 - the chromophore and emitter are linked in the same molecule via a twisted π -conjugated system; and
 - energy can transfer between the chromophore and emitter via the π -conjugated system.
14. The method of claim 13, wherein the chromophore is a perylene, an anthracene, a tetracene, a fluorescein, or a BODIPY.
15. The method of claim 13, wherein the chromophore is an anthracene.
16. The method of claim 13, wherein the emitter is a fluorescein, a rhodamine, a BODIPY, a squareine, a cyanine dye.
17. The method of claim 13, wherein the emitter is a BODIPY.
18. The method of claim 13, wherein the dye further comprises a functional group useful for attaching the label to the biomolecule.
19. The method of claim 13, wherein the dye further comprises a succinimidyl ester group.
20. A method of labeling a biomolecule, the method comprising contacting a biomolecule and a fluorescent dye to prepare a labeled biomolecule, wherein:
- the dye comprises a UV absorbing chromophore and a fluorescent emitter;
 - the chromophore and fluorescent emitter are conjugated to each other such that energy transfer between the chromophore and the fluorescent emitter comprises transfer via a through bond mechanism; and

the UV chromophore absorbs energy at a lower wavelength than that emitted by the fluorescent emitter.

21. The method of claim 20, wherein the chromophore is a perylene, an anthracene, a tetracene, a fluorescein, or a BODIPY.
22. The method of claim 20, wherein the chromophore absorbs energy at a maximum of about 266 nanometers.
23. The method of claim 20, wherein the emitter is a fluorescein, a rhodamine, a BODIPY, a squareine, or a cyanine dye.
24. The method of claim 20, wherein the dye further comprises a functional group suitable for covalently attaching the dye to the biomolecule.
25. The method of claim 20, wherein the dye further comprises a bromine group, a succinimidyl ester group, or a carboxylic acid group.
26. The method of claim 20, wherein the dye further comprises a succinimidyl ester group.
27. The method of claim 20, wherein the biomolecule is a nucleic acid.
28. The method of claim 20, wherein the biomolecule is DNA.
29. The method of claim 20, wherein the biomolecule is RNA.
30. The method of claim 20, wherein the biomolecule is a ddNTP.
31. The method of claim 20, wherein the biomolecule is a protein.
32. The method of claim 20, wherein the biomolecule is a peptide.
33. A method of labeling a biomolecule, the method comprising contacting a biomolecule and a fluorescent dye to prepare a labeled biomolecule, wherein:
the dye comprises an anthracene derivative and a BODIPY fragment; and
the anthracene derivative and the BODIPY fragment are conjugated to each other.
34. The method of claim 33, wherein the biomolecule is a nucleic acid.
35. The method of claim 33, wherein the biomolecule is DNA.
36. The method of claim 33, wherein the biomolecule is RNA.
37. The method of claim 33, wherein the biomolecule is a ddNTP.
38. The method of claim 33, wherein the biomolecule is a protein.
39. The method of claim 33, wherein the biomolecule is a peptide.
40. The method of claim 33, wherein:
the dye further comprises a chromophore; and

the chromophore and the anthracene derivative absorb in mutually exclusive regions of the UV spectrum.

41. The method of claim 33, wherein the dye further comprises a functional group suitable for covalently attaching the dye to the biomolecule.
42. The method of claim 33, wherein the dye further comprises a bromine group, a succinimidyl ester group, or a carboxylic acid group.
43. The method of claim 33, wherein the dye further comprises a succinimidyl ester group.
44. A method of detecting a biomolecule, the method comprising:
contacting a biomolecule and a fluorescent dye to prepare a labeled biomolecule; and
detecting the labeled biomolecule; wherein:
the dye comprises a UV absorbing chromophore and a fluorescent emitter;
the chromophore and fluorescent emitter are conjugated to each other such that energy transfer between the chromophore and the fluorescent emitter comprises transfer via a through bond mechanism; and
the UV chromophore absorbs energy at a lower wavelength than that emitted by the fluorescent emitter.
45. The method of claim 44, wherein the chromophore is a perylene, an anthracene, a tetracene, a fluorescein, or a BODIPY.
46. The method of claim 44, wherein the chromophore is an anthracene.
47. The method of claim 44, wherein the chromophore absorbs energy at a maximum of about 266 nanometers.
48. The method of claim 44, wherein the emitter is a fluorescein, a rhodamine, a BODIPY, a squareine, or a cyanine dye.
49. The method of claim 44, wherein the emitter is a BODIPY.
50. The method of claim 44, wherein the dye further comprises a functional group suitable for covalently attaching the dye to the biomolecule.
51. The method of claim 44, wherein the dye further comprises a bromine group, a succinimidyl ester group, or a carboxylic acid group.
52. The method of claim 44, wherein the dye further comprises a succinimidyl ester group.
53. The method of claim 44, wherein the biomolecule is a nucleic acid.
54. The method of claim 44, wherein the biomolecule is DNA.

55. The method of claim 44, wherein the biomolecule is RNA.
56. The method of claim 44, wherein the biomolecule is a ddNTP.
57. The method of claim 44, wherein the biomolecule is a protein.
58. The method of claim 44, wherein the biomolecule is a peptide.--

REMARKS

Claims 1-12 were prosecuted in the parent case, application Serial No. 09/460,178 and thus have been cancelled from this divisional application. The parent application was allowed on May 21, 2001, but has not yet issued.

The active claims in this case are claims 13-58.

The specification has been amended to recite the relationship with the parent case, namely that it is a divisional application.

Applicants do not believe that any fees are due at this time; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to this document, the Assistant Commissioner is authorized to deduct the fees from Baker Botts, L.L.P. Deposit Account No. 02-0383.

Respectfully submitted,



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June 13, 2001

FOETED 29903350

Marked up version of replacement paragraphs

This application is a divisional application of co-pending U.S. Patent Application Serial No. 09/430,718 filed on December 14, 1999, which claims the benefit of United States Provisional Patent Application entitled "Through Bond Energy Transfer in Fluorescent Dyes for Labelling Biological Molecules," Serial No. 60/112,711 filed December 18, 1998.

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